REMARKS

The present application is directed to attenuation of cancer by administering Group B β-hemolytic *Streptococci* (GBS) toxin receptors, or immunogenic fragments thereof, and is directed to related compositions and methods of producing the compositions. Claims 1, 29-30, 32, 35, 40-41, 44-48 and 55 are currently amended. No new matter is added and support for the amendments can be found throughout the specification and in the original claims. Claims 1, 4-16, 29-38, 40-48, and 55-56 will be pending upon entry of the amendments. It is applicant's understanding that the amendments submitted on February 6, 2006 were not entered.

Election/Restriction

Applicant wishes to thank the Examiner for rejoining Groups 1 and 11 from the Restriction Requirement of May 21, 2002, and withdrawing the requirement to elect a species.

Notice of Non-Responsive Amendment

A Notice of Non-Responsive Amendment was mailed on April 20, 2006, stating that the amendment filed February 6, 2006, presented claims drawn to a non-elected invention. Applicants respectfully submit that the claims as currently amended are drawn to the elected invention of Group 11 as set forth in the Restriction and Election Requirement of May 21, 2002.

Claim Rejections under 35 U.S.C. § 112, First Paragraph (Enablement)

In the Office Action mailed September 6, 2005, the Examiner maintained the rejection of Claims 1, 4-16, 30-38, 40-48, and 55-56 under 35 U.S.C. §112, first paragraph, for lack of enablement. Applicant respectfully traverse the rejection and request its withdrawal for the following reasons.

The Examiner cites several publications for the proposition that rodent models may not represent clinical efficacy in humans. Applicant agrees that, although many of the newly

cited publications recognize the value of mouse models, some call for the careful selection of such models and require that certain limitations be taken into account when predicting the efficacy of preclinical animal-tested cancer therapies in humans. However, applicant respectfully submits that U.S. Patent laws fail to require a rigorous correlation between animal models and the success of the claimed method in humans. See *Cross v. Iizuka*, 753 F.2d 1040, 1050 (Fed. Cir. 1985). A demonstration of the effectiveness of a drug is not required for obtaining a patent. See *In re Brana*, 51 F.3d 1560, 1567 (Fed. Cir. 1995). Applicant respectfully asserts that the disclosure provided in the specification of the present application enables one skilled in the art to make and use the GBS toxin receptor compositions and methods having an amino acid sequence substantially identical to HP59 or SP55 as claimed.

Applicant submitted with the Response filed February 6, 2006, a Second Declaration of Carl Hellerqvist under 37 C.F.R. §1.132. For the Examiner's convenience, an additional copy of the Second Declaration of Carl Hellerqvist is submitted herewith. This Declaration concludes that observations in appropriately selected mouse models reasonably correlate with observations in other mammals, such as humans. Applicant respectfully asserts that the mouse models used in the Examples of the present application were selected so they reasonably correlate with human pathological angiogenesis to demonstrate the ability of GBS toxin receptors having an amino acid sequence substantially identical to HP59 or SP55 to attenuate cancer in a mammal as now claimed.

The enclosed Declaration describes multiple studies in which applicant demonstrated the correlation of the effects of GBS toxin administration in both mouse cancer models and human patients. By cloning and identifying HP59, the target protein for GBS toxin/CM101 in humans and sheep, and by immunohistochemical studies in mice, applicant showed the existence of a conserved molecular marker for neonatal and pathologic vasculature in mammals. See Fu *et al.* (2001). Applicant also showed that HP59 is present in the tumor vasculature independently of site and type. See Table 1 in Fu *et al.* All antibodies generated to the human and sheep HP59 analogue cross-reacted with pathologic vasculature in mice.

Thus, the HP59 protein is a pathologic vasculature target common between humans, sheep and mice.

As further discussed in the enclosed Declaration, applicant showed that administration of HP59 protein generates a cellular immune response that inhibits pathologic angiogenesis. Thus, applicant identified HP59 as a target for attenuating cancer by inhibiting the associated pathological angiogenesis.

It is applicant's position that, in the field of cancer vaccines, mouse models are considered to correlate reasonably well with human pathological angiogenesis conditions, such as those associated with cancer. Although the Examiner cited several publications in the present Office Action as evidence against applicant's position, the cited publications predominantly focus on the limitations of mouse models for predicting clinical outcomes during development of drugs targeting various tumor-specific targets, not treatments directed at pathological vasculature-specific targets. For example, Wang *et al.* (2001), cited by the Examiner, describes the use of anti-cancer vaccines against tumor-specific antigens. Accordingly, the cited publications are not relevant to applicant's claimed method.

Genetic and phenotypical diversity of tumor tissues makes tumor-specific targeting difficult. This diversity negatively influences the correlation between mouse models and humans when tumor targets are affected. In contrast, one of ordinary skill in the art expects reasonable correlation between animal models and humans when targeting cancer-associated pathologic vasculature, provided that the vascular target is common in the model animal and humans. At least one reason for the expected reasonable correlation between animal models and humans when testing therapies that target pathologic vasculature is that such vasculature is relatively genetically and phenotypically homogenous. Applicant selected a mouse model to demonstrate the claimed methods because mouse vasculature possesses the same target as human and sheep vasculature. Therefore, one of ordinary skill in the art would expect that the mouse models utilized in the present application would reasonably correlate with human results for the purpose of observing attenuation of cancer through inhibition of angiogenesis in accordance with applicant's method.

In the present application, applicant's method and compositions target a protein common to the pathologic vasculature of various types of tumors and shared by at least humans, mice, and sheep. Applicant also elucidated the common mechanism of action of GBS toxin during angiogenesis. Based on the foregoing and on the previously submitted arguments, applicant maintains that the attenuation of cancer through targeting the associated pathological angiogenesis is shown in the mouse models used and in the working examples of the present application. Due to the common pathological angiogenesis vascular target shared between humans and mice, the use of a mouse model reasonably correlates with and is generally predictive of the ability to attenuate cancer in a human by targeting the associated pathological angiogenesis. For at least the foregoing reasons, applicant respectfully requests withdrawal the rejection under 35 U.S.C. § 112, first paragraph.

Claim Rejections under 35 USC §112, Second Paragraph

In the Office Action mailed September 6, 2005, the Examiner rejected Claims 1, 4-16, 29-38, 40-48, 55 and 56 under 35 USC §112, second paragraph, as indefinite. Applicant respectfully submits that the amendments to the claims overcome the rejection.

In particular, the Examiner rejected the claims on the basis that the language "wherein the pathoangiogenic condition comprises cancer" was indefinite. Claims 1, 30, and 55 have been amended to be drawn to a method and a composition for attenuating cancer. Support for the amendments can be found on page 7, lines 8-13 and page 10, lines 5-13.

In addition, the Examiner rejected the claims on the basis that the language "comprises HP59 or SP55" was indefinite. Claims 1, 29, 30 and 55 have been amended to clarify that the Group B β-hemolytic *Streptococci* toxin receptor has an amino acid sequence substantially identical to HP59 or SP55, or immunogenic fragment thereof. Support for this amendment is found at least on p. 8, line 28, through p. 9, line 25.

For at least the foregoing reasons, applicant asserts that claim amendments overcome the rejection under 35 U.S.C. §112, second paragraph, as indefinite and requests withdrawal thereof.

Rejections under 35 USC §112, First Paragraph (Written Description)

The Examiner rejected Claims 1, 4-16, 29-38, 40-48, 55 and 56 under 35 USC §112, first paragraph, as failing to comply with the written description requirement on the basis that the specification does not support the genus of polypeptides of GBS toxin receptors or immunogenic fragments thereof as recited in the rejected claims.

As discussed above, applicant has amended the claims to clarify that the GBS toxin receptor has an amino acid sequence substantially identical to HP59 or SP55. Applicant asserts that the specification provides sufficient written description for the genus recited in the claims by providing a description of a representative number of species, by actual reduction to practice, and by disclosure of relevant, identifying characteristics sufficient to show that applicant was in possession of the claimed genus. Applicant disclosed the amino acid and nucleic acid sequences for HP59 and SP55 (see Table 1 in the specification), two Group B β-hemolytic *Streptococci* toxin receptors whose features are defined, for example, on page 6, lines 26-30 of the specification. Applicant described how to identify other GBS toxin receptors using the HP59 and SP55 nucleic acid sequences on page 19, line 14, through page 22 of the specification.

The HP59 and SP55 nucleic acid sequences provided in the present application are relevant characteristics that allow one of ordinary skill in the art to readily identify other members of the genus of Group B β-hemolytic *Streptococci* toxin receptor substantially identical to HP59 or SP55. Accordingly, the specification provides sufficient written description for the genus of Group B β-hemolytic *Streptococci* toxin receptors substantially identical to HP59 or SP55. The specification also provides sufficient written description for the genus of the immunogenic GBS toxin receptor fragments. Specifically, in Tables 3 and 4, a number of immunogenic peptides (Hab 1, Hab2, Hab 3, Hab 4, p55a, p56a and p57) are provided. Table 2 provides three more regions of SP55 that are likely to be immunogenic.

Accordingly, applicant respectfully asserts that the specification of the present application in combination with knowledge available to one of ordinary skill in the art at the time of filing of the present application would reasonably convey to the skilled artisan that applicant had possession of the claimed invention at the time the application was filed. For

at least the foregoing reasons, applicant respectfully requests withdrawal of the rejection under 35 U.S.C. §112, first paragraph, as failing to comply with a written description requirement.

Rejection of Claims under 35 USC §102(e)

Claims 29-34, 37, 38, 40-43, 45-48, 55, and 56 were rejected by the Examiner under 35 U.S.C. §102(e) as anticipated by U.S. Patent No. 6,803,448 ("the '448 patent") to Carl G. Hellerqvist and Changlin Fu. Applicant respectfully submits that the '448 patent is not a valid prior art reference

Applicant submitted with the Response filed February 6, 2006, a "*Petition for Unintentionally Delayed Claim of Benefit of Earlier Filing Date*" to claim the benefit of currently pending U.S. Patent Application Serial No. 10/823,506, which is a divisional application of U.S. Patent Application Serial No. 09/359,167, now issued as U.S. Patent No. 6,803,448. Accordingly, upon granting of the Petition, U.S. Patent No. 6,803,448 is not prior art within the meaning of 35 USC §102(e), and applicant requests withdrawal of the rejection.

Obviousness-type Double Patenting Rejection

The Examiner rejected Claims 29-32, 38, 40-43, 45-47 and 55 over U.S. Patent No. 6,803,448 to Hellerqvist under the doctrine of obviousness-type double patenting. Applicant submits that, when allowable subject matter is found in the present application, applicant will file, if appropriate, a terminal disclaimer disclaiming the part of the term of a patent to issue from the present application extending beyond the term of U.S. Patent No. 6,803,448.

Other Issues

The Examiner appeared to require, on page 19 of the Office Action, a showing that the inventions claimed in the present application and in U.S. Patent No. 6,803,448 were commonly owned at the time of the invention in order to fulfill the provisions of 35 U.S.C. § 103(c) and 37 C.F.R. 1.78(c). Applicant submits that, upon granting of *A Petition for an*

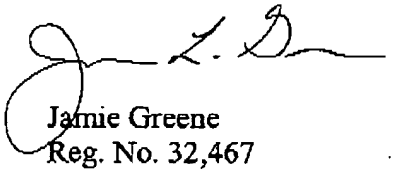
Unintentionally Delayed Claim of Benefit of Earlier Filing Date, this requirement will be moot. If applicant misunderstood the relevant section of the Office Action, clarification is respectfully requested.

CONCLUSION

Applicant is of the opinion that the Office Action has been completely responded to and that the application is now in condition for allowance. Such action is respectfully requested. No additional fees are believed due, however, the Commissioner is hereby authorized to charge any deficiencies that may be required or credit any overpayment to Deposit Account Number 11-0855.

If the Examiner believes any informalities remain in the application that may be corrected by Examiner's Amendment, or there are any other issues that can be resolved by telephone interview, a telephone call to the undersigned at (404) 745-2473 is respectfully solicited.

Respectfully submitted,



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